Armed Forces College of Medicine

AFCM

Digestion and absorption of fat

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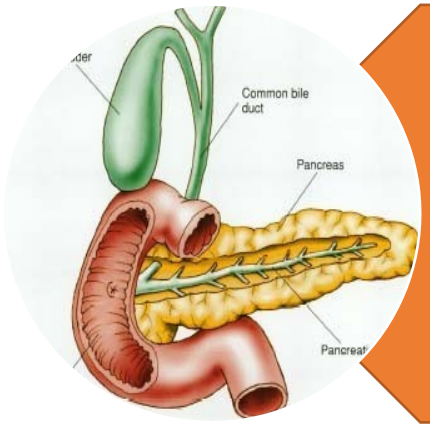
Lecture key points



Digestion of fats

Clinical significance

INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

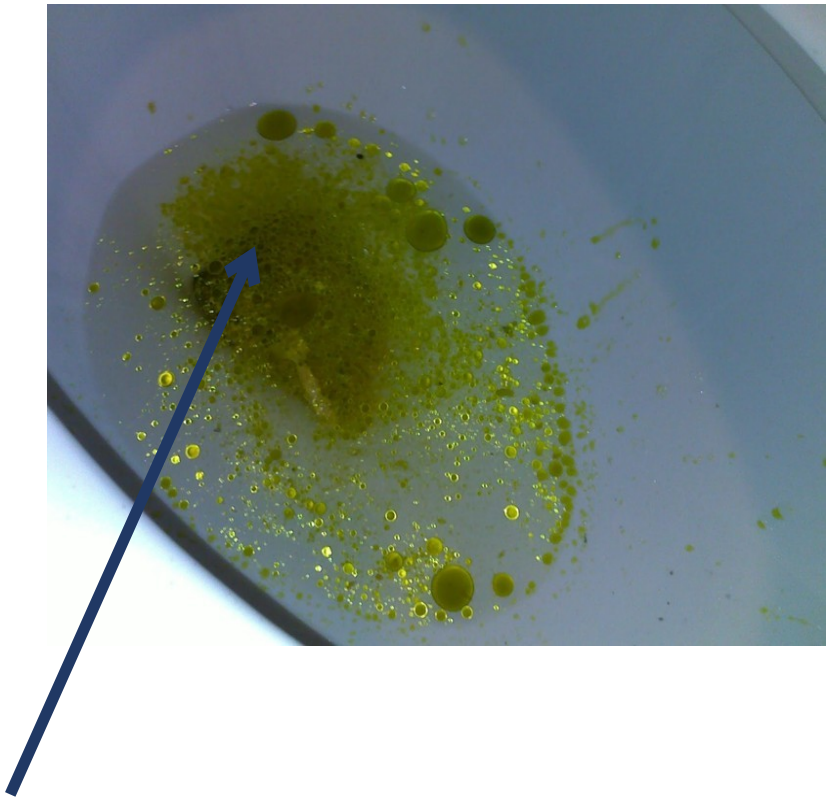
1-Summarize the phases of digestion and absorption of fat

2. Distinguish different enzymes needed for fat digestion

3. Interpret biochemical basis of steatorrhea

Clinical case scenario

- A 15-year-old girl presents to the physician's office with a 6 months history of intermittent **diarrhea**.
- She is underweight but not cachectic. A stool examination is **negative for blood**. The 72-hour fecal fat study shows a **moderate increase in fat content**. A complete blood count (CBC) shows a mild anemia. Her iron studies indicate the presence of iron deficiency.
- Her small size, the **steatorrhea and the iron deficiency all suggest the possibility of some type of GIT malabsorption condition**.



Dietary fats

- **Saturated fats (90%): triacylglycerol ([TAG],cholesterol, cholesterol esters**
- **Unsaturated fats:**
  - Monounsaturated fatty acids (**MUFAs**)
  - Polyunsaturated **fats (**PUFAs).
- **Transfats : According to World Health Organization (WHO)**

Types of Fatty Acids	Examples of Sources	Health Impacts and Intake Recommendations
Saturated  • No double bond • Straight structure • Solid at room temperature	 Beef Butter Coconut oil	• Increase risk of heart disease • Less than 20g of saturated fats per day (for a 2000 kcal diet)
Trans  • One or more double bonds in trans configuration • Straight structure • Semi-solid/Solid at room temperature	 Margarine Cream soup with puff pastry Chicken pie	• Increase risk of heart disease • Less than 2.2g of trans fats per day (for a 2000 kcal diet)
Monounsaturated  • One double bond in cis configuration • Bent structure • Liquid at room temperature	 Olive oil Canola oil Peanut oil	• May reduce risk of heart disease • Moderate intake of monounsaturated fats
Polyunsaturated  • Multiple double bonds in cis configuration • Even more "bent" in structure • Liquid at room temperature	 Soybean oil Corn oil Fatty fish	• May reduce risk of heart disease • Moderate intake of polyunsaturated fats

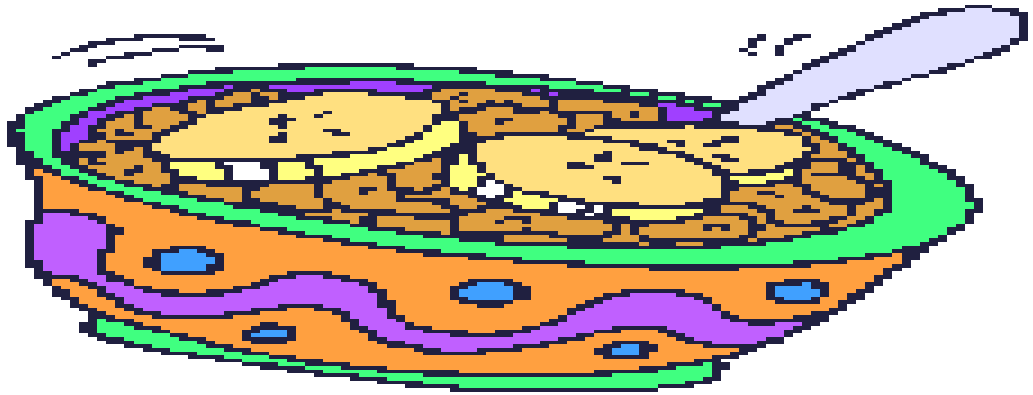
Outlines of fats Digestion

A-Digestion (hydrolysis)

(in stomach & intestine)

B-Emulsification of dietary lipid in the small intestine

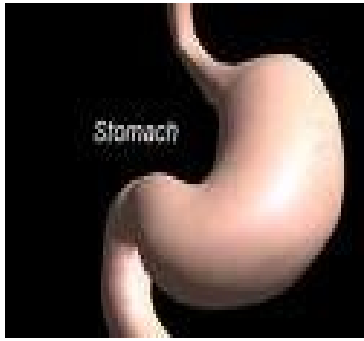
(duodenum)



1-Processing of dietary lipid in the stomac

A-Digestion (hydrolysis) in stomach

The digestion of lipids begins in the stomach, by an acid-stable lipase (lingual and gastric).



- Lingual and gastric Lipases has optimums pH of 4 to 6 .
- They degrade TAG with short to medium –FA (fewer than 12 carbons) (milk).
- So it is has little significance in adult human because it is activated by pH of the adult human stomach (more acidic than neonates)

Explain on biochemical basis importance of Lingual and gastric Lipases

Play a particularly important role in:

- **Lipid digestion in neonates, as the milk fat is the primary source of calories.**
- **They also become important digestive enzymes in individuals with pancreatic insufficiency such as those with cystic fibrosis (CF). There is a defect in Chloride channels which leads to the depletion of water on the cell surface results in thickened secretions that clog or obstruct the pancreatic ducts, preventing pancreatic enzymes from reaching the intestine. Thus, Lingual and gastric lipases aid these patients in degrading TAG molecules (especially those with short- to medium-chain length fatty acids as in milk) despite a near or complete absence of pancreatic lipase.**

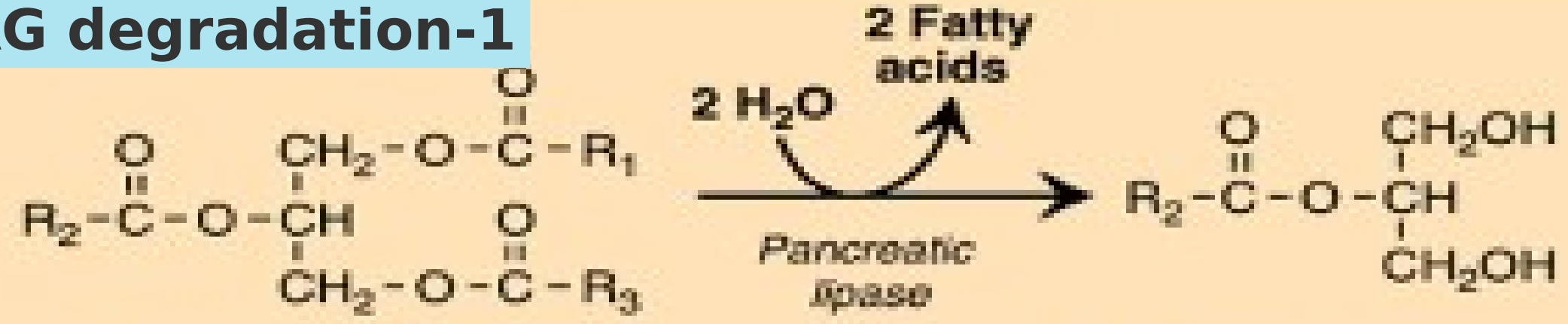
B. Emulsification of dietary lipid in the small intestine (duodenum)

- Bile salts, made in the liver and stored in the gallbladder.
- occurs mainly in the duodenum.
- Emulsification increases the surface area of the hydrophobic lipid droplets so that the digestive enzymes can act effectively.
- Emulsification is done by two complementary mechanisms:
  - Conjugated bile salts
  - Mechanical mixing due to peristalsis

C. Degradation of dietary lipids by pancreatic enzymes

The dietary TAG, CE, and PL are degraded mainly by pancreatic enzymes.

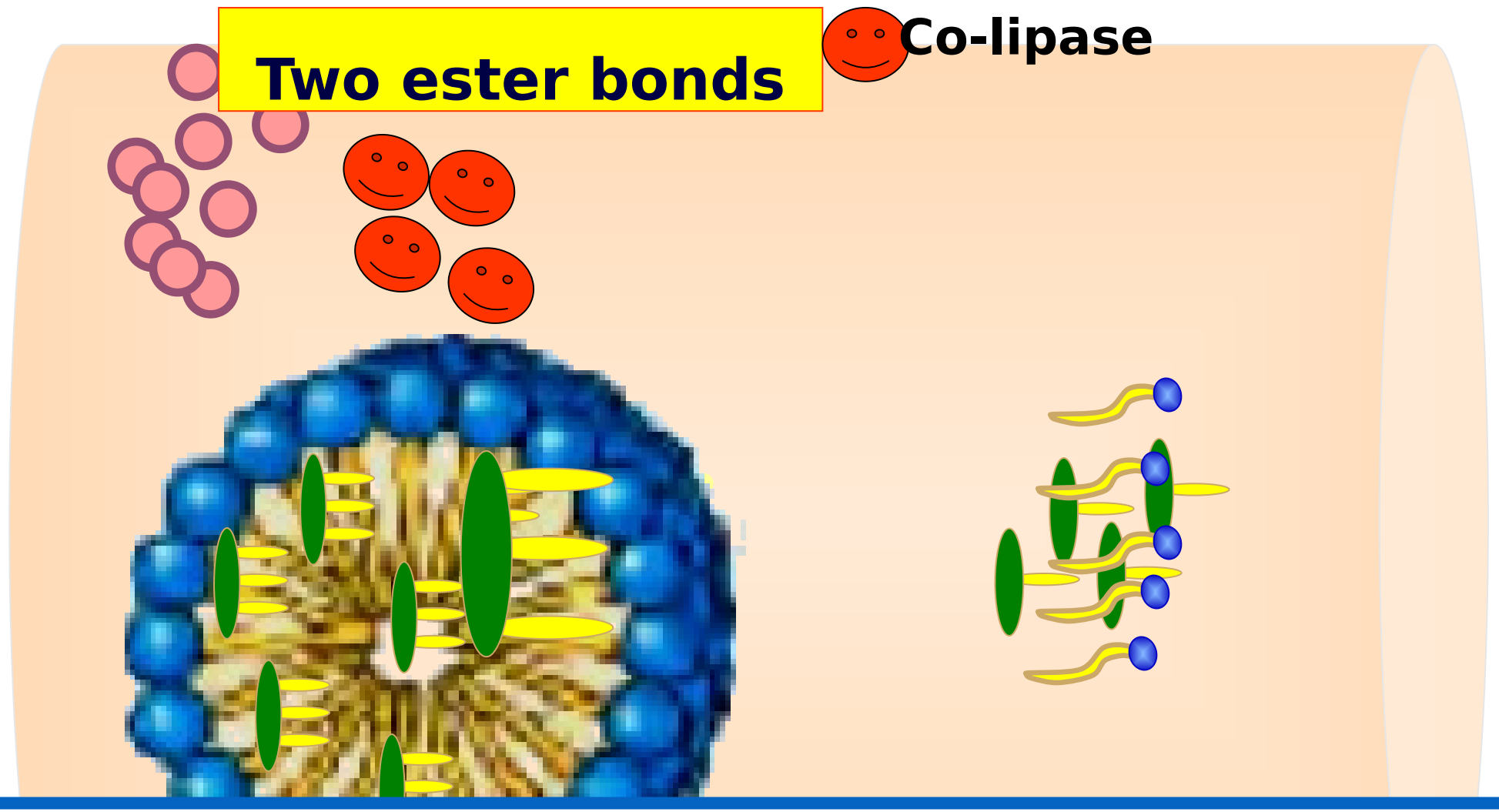
TAG degradation-1



++bile salts + Ca

- **TAG molecules are too large to be taken up efficiently by the mucosal cells of the intestinal villi. Therefore,** *pancreatic lipase* **,which preferentially removes** FA at C1 & C3 giving 2-MAG + 2FFA

The *pancreatic lipase* needs colipase (a small protein secreted by pancreas) to be active



Explain on biochemical basis mechanism of action of Orlistat as anti obesity drug

- Orlistat, an anti obesity drug, inhibits gastric and pancreatic lipases, thereby

Mechanism of action of Orlistat Quiz (USMLE)

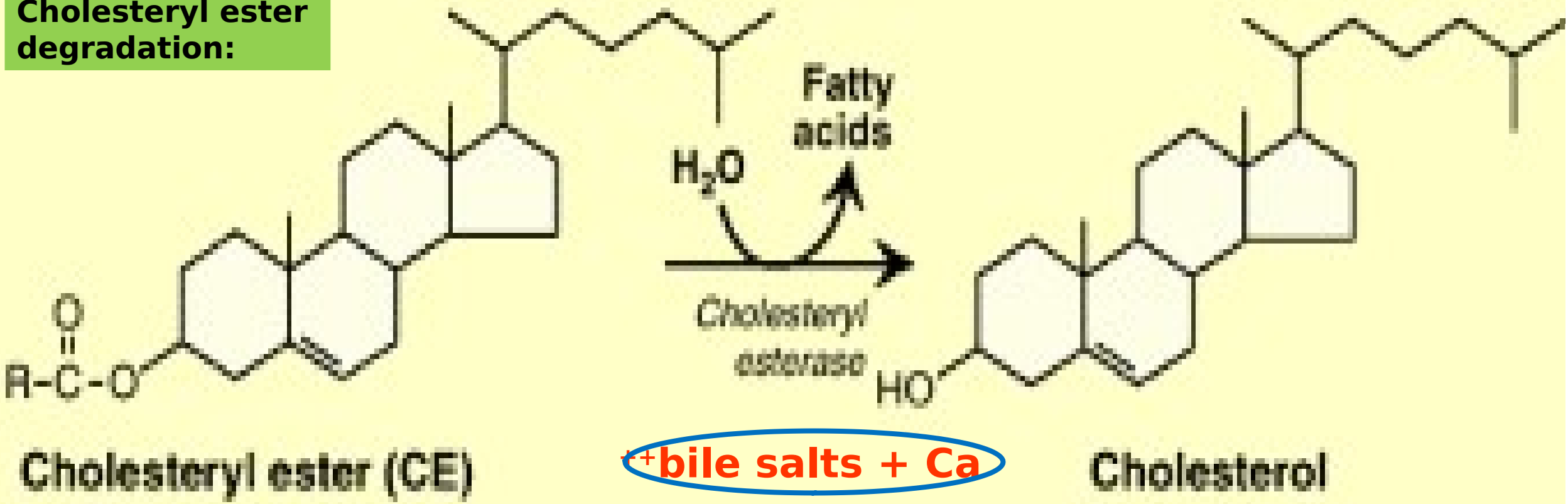
A 32- year- old male reported to emergency with active bleeding from nose. History revealed that he had been on Orlistat for weight reduction from the past two years. He had started Orlistat without the advice of any practitioner and had lost nearly 20 kg of body weight .There was no history of hypertension, bleeding disorder or any other medical illness.No such bleeding episode occurred in the past.

There was no abnormality detected upon local examination of nose. What is the relationship between Orlistat and epistaxis?

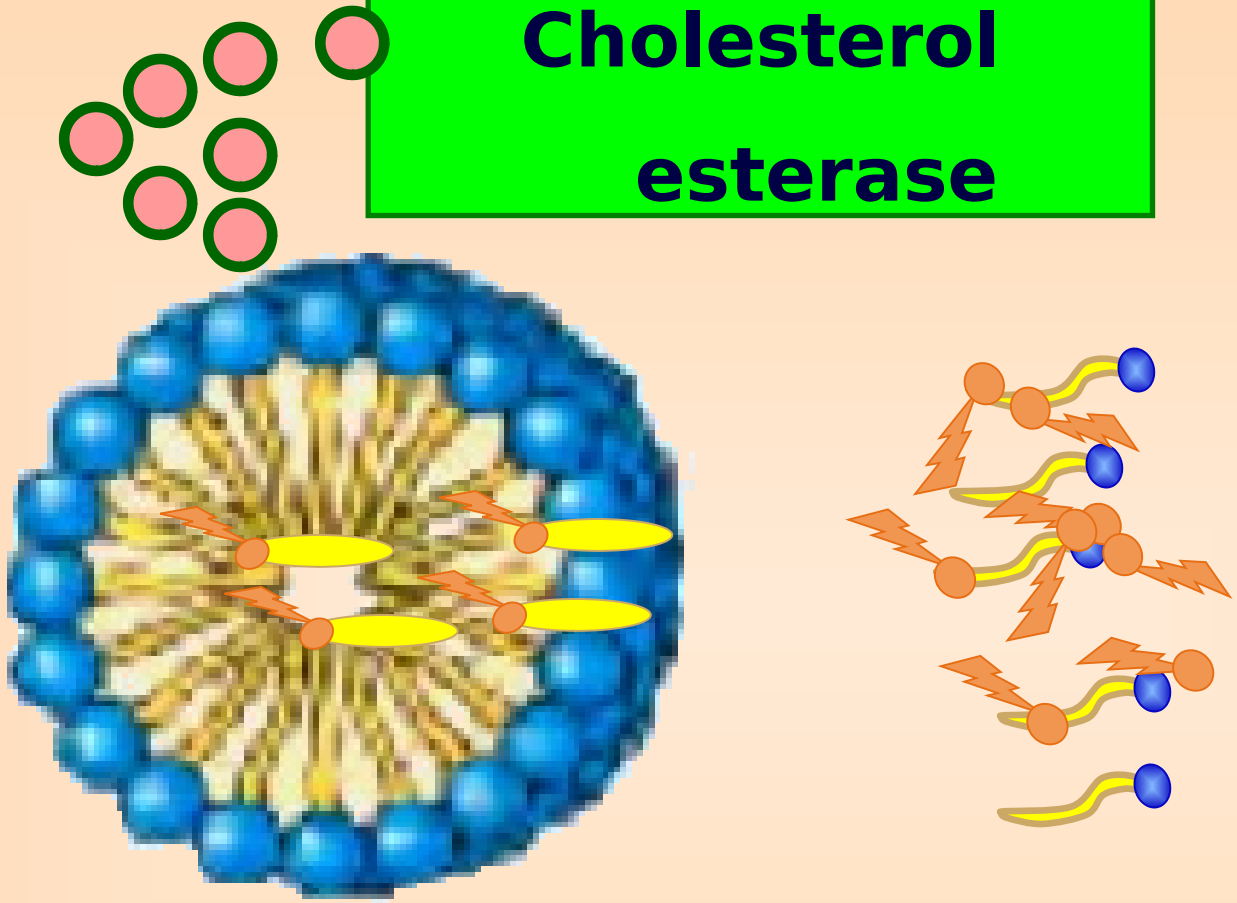
:Cholesteryl ester degradation-2

Most cholesterol is free, 10–15% is CE. Pancreatic cholesteryl esterase gives free fatty acids + Cholesterol.

Cholesteryl ester degradation:



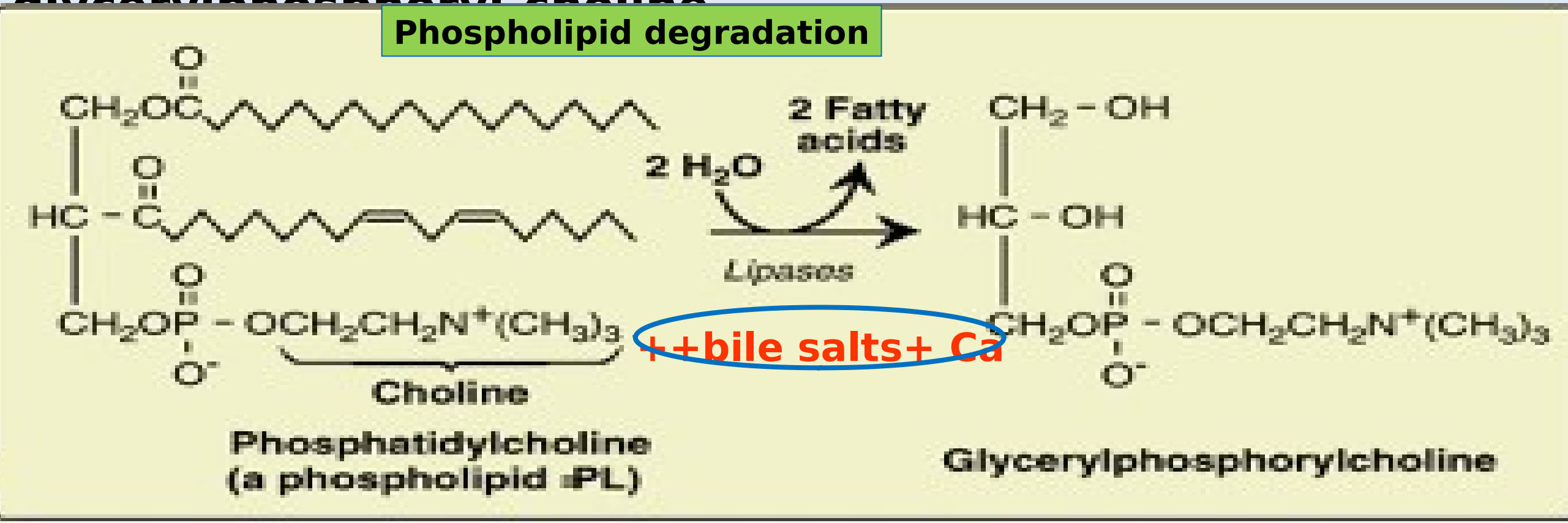
Cholesterol esterase



:Phospholipid degradation-3

Phospholipase A_2 (PLA_2) removes (C_2 FA) giving lyso-phospholipid.

(C_1 FA) is then removed by lyso-phospholipase, giving a



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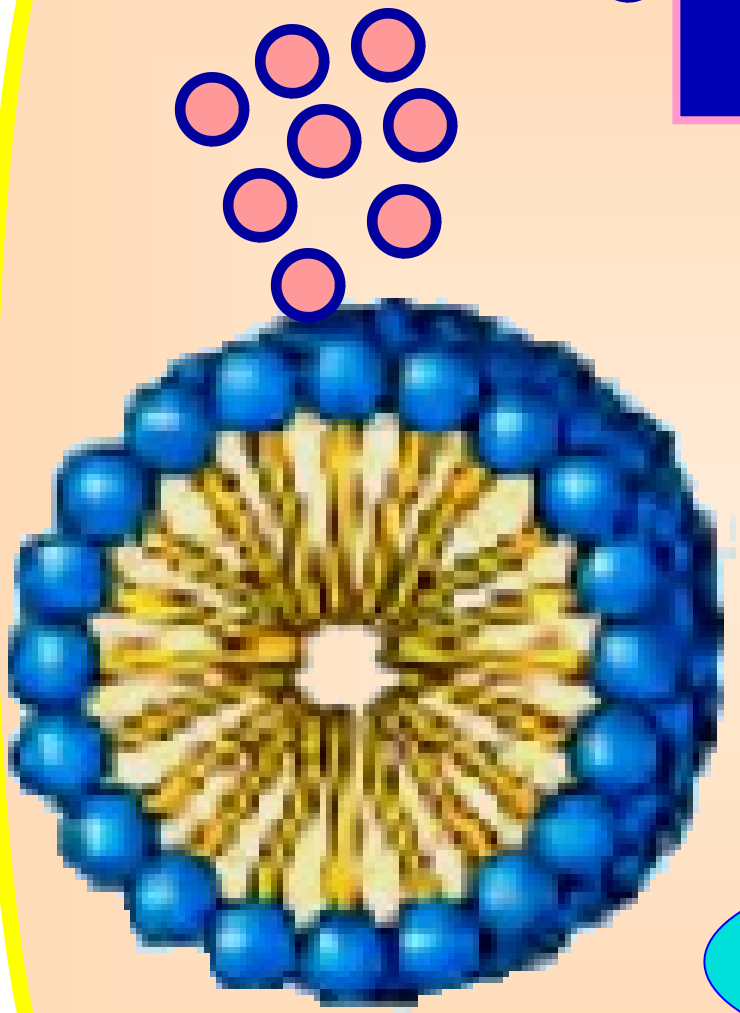
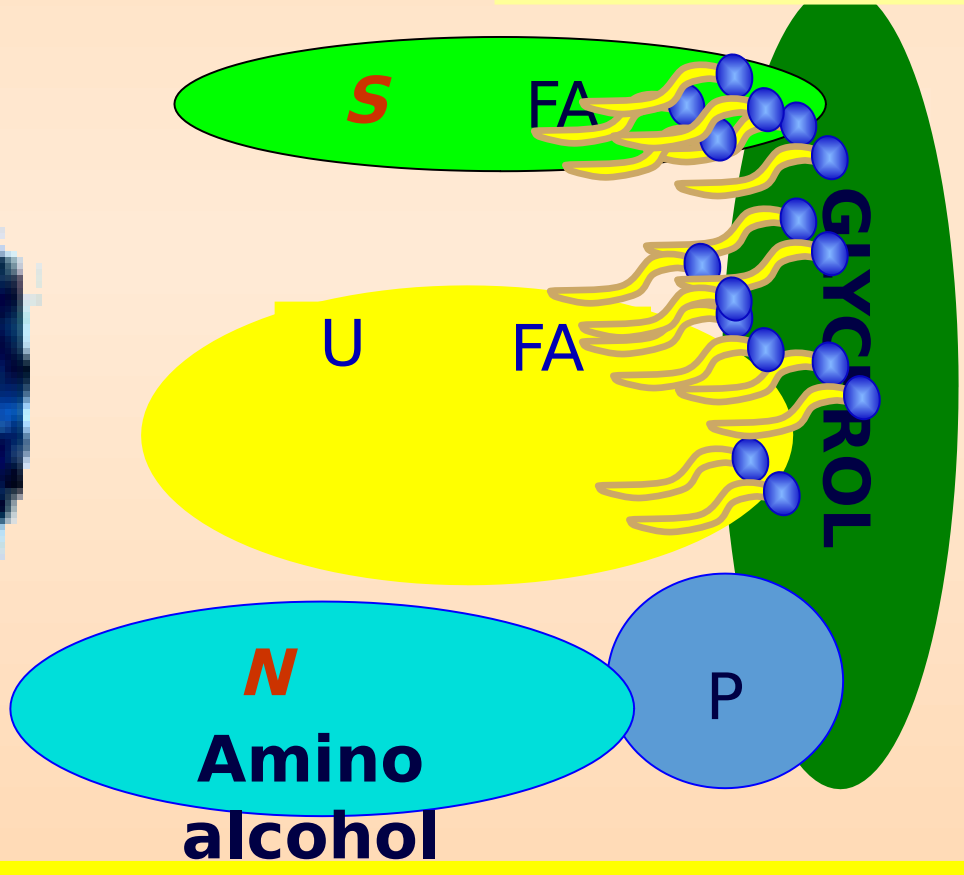
Phospholipase A2



Glycero phosphoryl base



Digestion of lipids Quiz (USMLE)

Which one of the following statements about the digestion of lipids is correct?

A. **Large lipid droplets are emulsified (have their surface area increased) in the mouth through the act of chewing (mastication).**

B. The enzyme colipase facilitates the binding of bile salts to mixed micelles,maximizing the activity of pancreatic lipase.

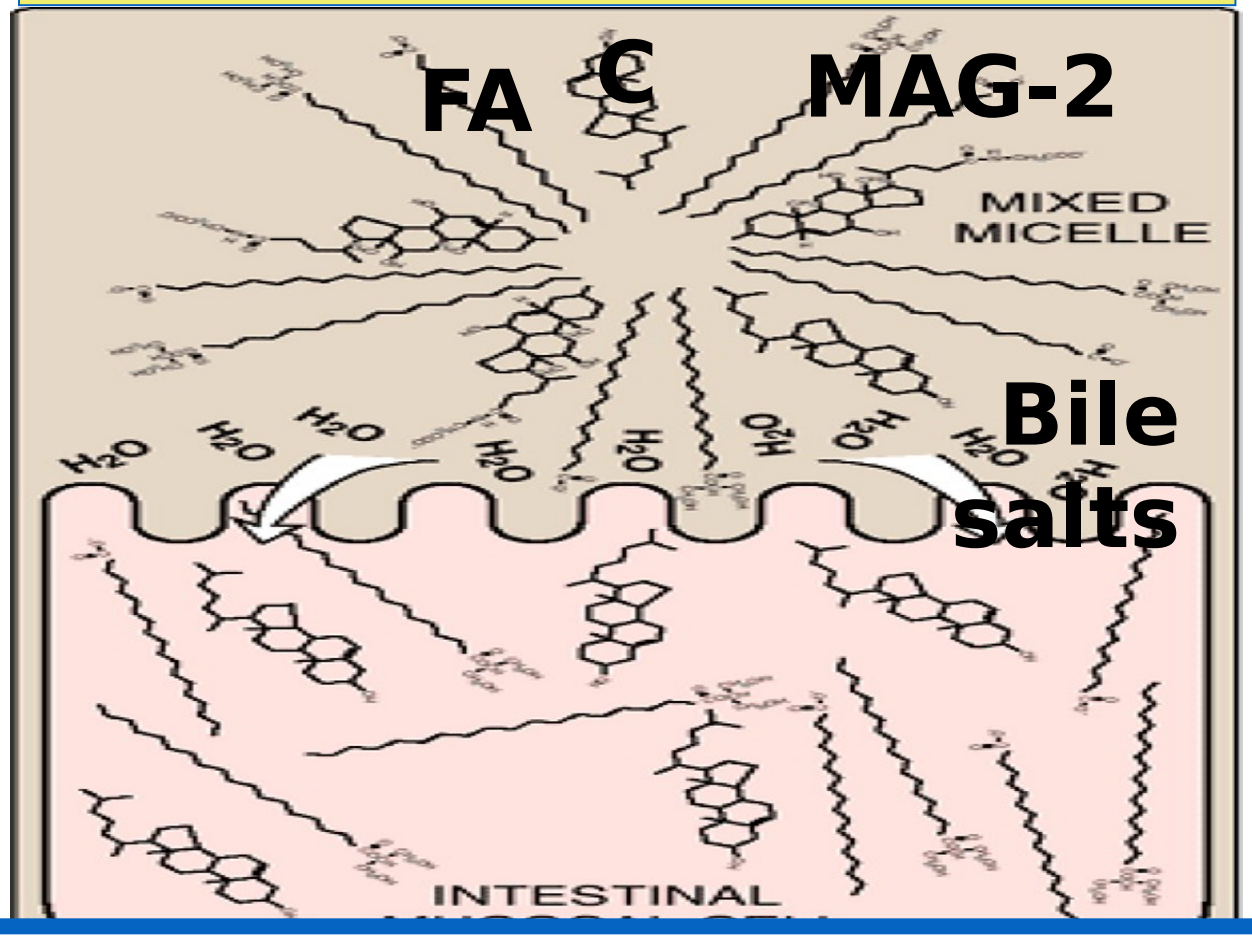
C. The peptide hormone secretin causes the gallbladder to contract and release bile.

D. Patients with cystic fibrosis have difficulties with digestion because their thickened pancreatic secretions are less able to reach the small intestine, the primary site of lipid digestion.

E. Formation of triacylglycerol-rich chylomicrons is independent of protein synthesis in the intestinal mucosa.

Absorption of lipids by intestinal mucosal cells, or enterocytes:

II. Solubilization in micelles



Micelles are disk shaped clusters of amphipathic lipids= [inside hydrophobic & hydrophilic outside] Therefore Are soluble in aqueous environment of the intestine.

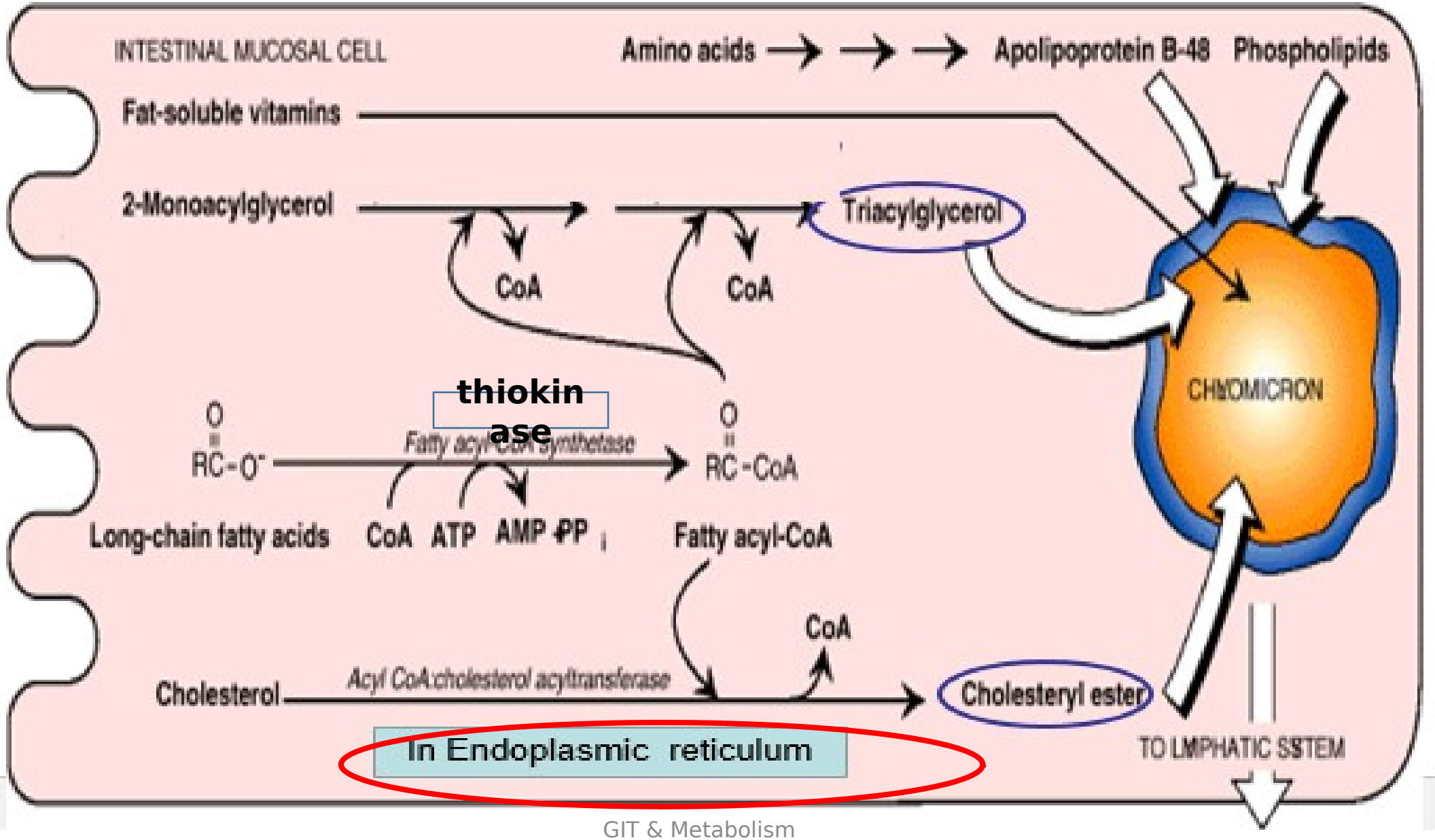
- **Micelles contains: digestion product of lipids (Free fatty acids, free cholesterol, and 2-monoacylglycerol are the primary products of lipid digestion in the jejunum. These, plus bile salts and fat-soluble vitamins (A, D, E,and K).**

Absorption of lipids by intestinal mucosal cells, or enterocytes:

- Relative to other dietary lipids, **cholesterol is only poorly** absorbed by the enterocytes.

- Drug therapy (for example, with **ezetimibe**) can further reduce cholesterol absorption in the small intestine.]
- **Short- and medium-chain** length fatty acids are **water soluble** and, thus, do not require the assistance of mixed micelles for absorption by the intestinal mucosa.

III-uptake by enterocytes & Resynthesis (Absorption)



IV- Incorporation in chylomicron (Secretion)

TAGs and CE are-
.very hydrophobic

-Apo-B48 stabilizes & increases the solubility.

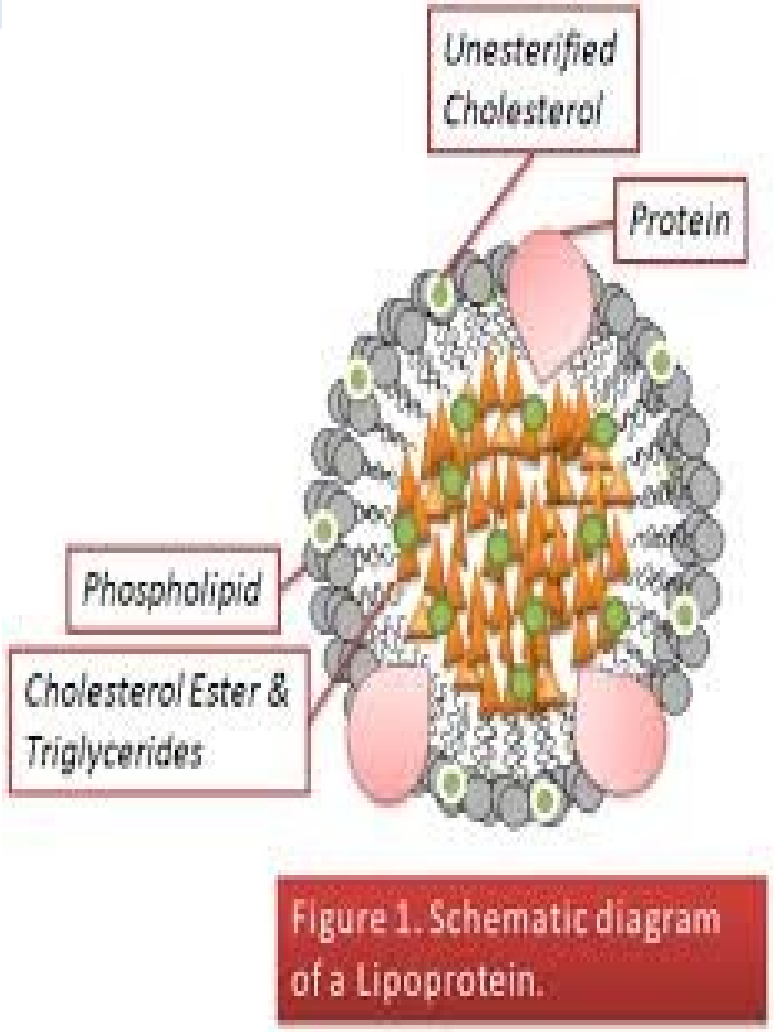


Figure 1. Schematic diagram of a Lipoprotein.

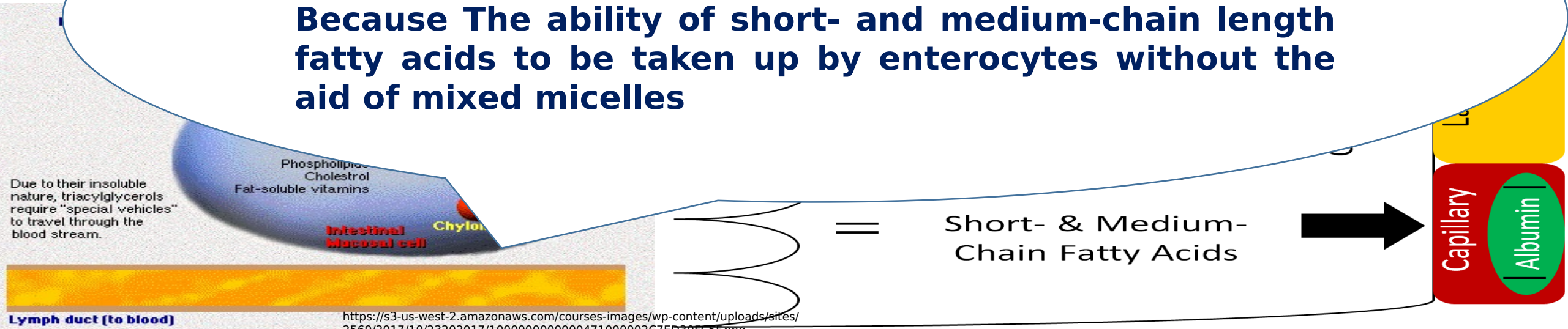
?How do dietary lipids reach blood

V- Exocytosis of chylomicron

Chylomicrons are released by exocytosis from enterocytes into lacteals of lymphatic system to the thoracic duct, and then finally to the blood causing turbidity.
This is known: Post-alimentary hyperlipidemia.

Explain on biochemical basis dietary therapy of short- and medium-chain in lipid malabsorption conditions

Because The ability of short- and medium-chain length fatty acids to be taken up by enterocytes without the aid of mixed micelles



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Absorption of lipids Quiz (USMLE)

Which one of the following statements about the absorption of lipids from the intestine is correct?

A. Dietary triacylglycerol must be completely hydrolyzed to free fatty acids and glycerol before absorption.

B. The triacylglycerol carried by chylomicrons is degraded by lipoprotein lipase to fatty acids that are taken up by muscle and adipose tissues and glycerol that is taken up by the liver.

C. Fatty acids that contain fewer than 12 carbon atoms are absorbed and enter the

circulation primarily via the lymphatic system.

D. Deficiencies in the ability to absorb fat result in excessive amounts of chylomicrons in the blood.

Pathological Conditions affecting Fat Digestion and Absorption

,Fatty diarrhea, fatty stool .milky stool or Steatorrhea

Steatorrhea: is the presence of excess fat in feces

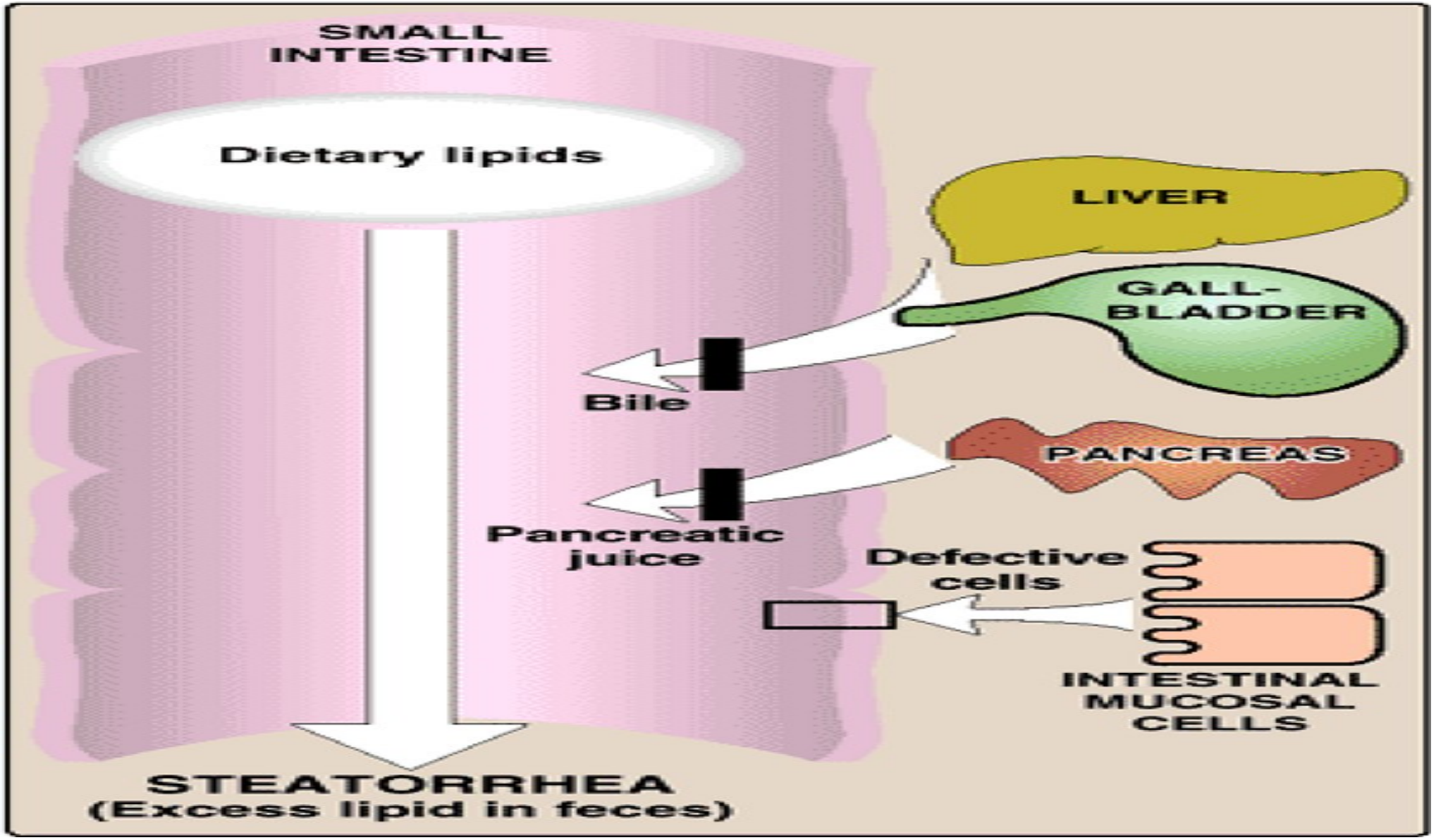
This occurs due to:

1-Deficiency of Pancreatic lipases or co-lipase e.g. pancreatitis…etc.

2-Deficiency of Bile salts e.g. Obstruction of bile duct (stone or cancer head of pancreas), cholecystitis and hepatitis or liver cell failure or hepatocellular carcinoma).

3-Any disease affecting intestinal absorption as gastroenteritis or malabsorption syndrome.

Causes of Steatorrhea



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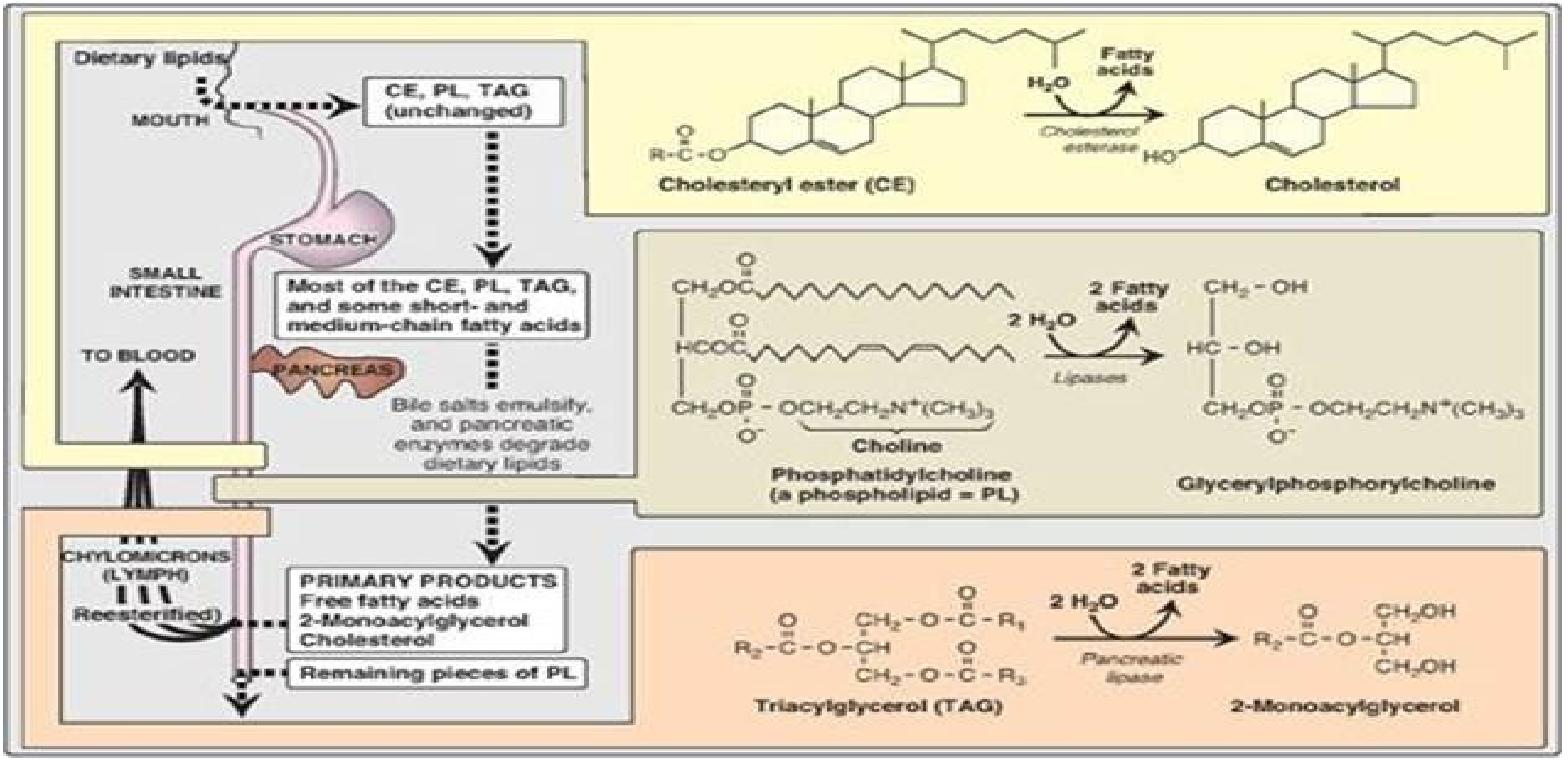
Lecture Summary (lipid digestion & absoerption)



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SUGGESTED TEXTBOOKS

- "Lippincott's Illustrated Reviews in Biochemistry" by P.C.Champe, R.A.Harvey and D.R.Ferrier
- "Harper's Biochemistry" by R.K.Murray, D.K.Granner, P.A. Mayes and V.W.Rodwell.
- Fundamentals of Clinical Chemistry (Tietz) Sixth
- "Textbook of Biochemistry with Clinical Correlations" by T.M.Devlin
- ***www.namrata.co- Biochemistry for medics***

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